

CLAIMS

1. An aglycosylated IgG antibody having a binding affinity for the CD3 antigen complex.
2. An aglycosylated antibody according to Claim 1, which has a binding affinity for the human CD3 antigen complex.
- 05 3. An aglycosylated antibody according to Claim 2, in which at least one CDR is selected from the amino acid sequences:
 - (a) Ser-Phe-Pro-Met-Ala,
 - (b) Thr-Ile-Ser-Thr-Ser-Gly-Gly-Arg-Thr-Tyr-Tyr-Arg-Asp-Ser-Val-Lys-Gly,
 - 10 (c) Phe-Arg-Gln-Tyr-Ser-Gly-Gly-Phe-Asp-Tyr,
 - (d) Thr-Leu-Ser-Ser-Gly-Asn-Ile-Glu-Asn-Asn-Tyr-Val-His,
 - (e) Asp-Asp-Asp-Lys-Arg-Pro-Asp,
 - (f) His-Ser-Tyr-Val-Ser-Ser-Phe-Asn-Val,and conservatively modified variants thereof.
- 15 4. An aglycosylated antibody according to Claim 2, which has a heavy chain with at least one CDR selected from the amino acid sequences:
 - (a) Ser-Phe-Pro-Met-Ala,
 - (b) Thr-Ile-Ser-Thr-Ser-Gly-Gly-Arg-Thr-Tyr-Tyr-Arg-Asp-Ser-Val-Lys-Gly,
 - 20 (c) Phe-Arg-Gln-Tyr-Ser-Gly-Gly-Phe-Asp-Tyr,and conservatively modified variants thereof, and/or a light chain with at least one CDR selected from the amino acid sequences:
 - (d) Thr-Leu-Ser-Ser-Gly-Asn-Ile-Glu-Asn-Asn-Tyr-Val-His,
 - 25 (e) Asp-Asp-Asp-Lys-Arg-Pro-Asp,
 - (f) His-Ser-Tyr-Val-Ser-Ser-Phe-Asn-Val,and conservatively modified variants thereof.
5. An aglycosylated antibody according to Claim 2, which has a heavy chain with three CDRs comprising the amino acid sequences:
 - 30 (a) Ser-Phe-Pro-Met-Ala,
 - (b) Thr-Ile-Ser-Thr-Ser-Gly-Gly-Arg-Thr-Tyr-Tyr-Arg-Asp-Ser-Val-Lys-Gly,
 - (c) Phe-Arg-Gln-Tyr-Ser-Gly-Gly-Phe-Asp-Tyr,

or conservatively modified variants thereof, and a light chain with three CDRs comprising the amino acid sequences:

(d) Thr-Leu-Ser-Ser-Gly-Asn-Ile-Glu-Asn-Asn-Tyr-Val-His,

(e) Asp-Asp-Asp-Lys-Arg-Pro-Asp,

(f) His-Ser-Tyr-Val-Ser-Ser-Phe-Asn-Val,

or conservatively modified variants thereof, the heavy chain CDRs being arranged in the order (a), (b), (c) in the leader → constant domain direction and the light chain CDRs being arranged in the order (d), (e), (f) in the leader → constant domain direction.

6. An aglycosylated antibody according to any of Claims 1 to 5, in which the variable domain framework regions are of or are derived from those of rat or mouse origin.

7. An aglycosylated antibody according to any of Claims 1 to 5, in which the CDRs are of different origin to the variable framework region.

8. An aglycosylated antibody according to Claim 7, in which the variable domain framework regions are of or are derived from those of human origin.

9. An aglycosylated antibody according to Claim 8, in which the heavy chain variable domain framework region reading from in the leader → constant domain direction comprises

Glu-Val-Gln-Leu-Leu-Glu-Ser-Gly-Gly-Gly-Leu-Val-Gln-Pro-Gly-Gly-Ser-Leu-Arg-Leu-Ser-Cys-Ala-Ala-Ser-Gly-Phe-Thr-Phe-Ser-/CDR/-
Trp-Val-Arg-Gln-Ala-Pro-Gly-Lys-Gly-Leu-Glu-Trp-Val-Ser-/CDR/-
Arg-Phe-Thr-Ile-Ser-Arg-Asp-Asn-Ser-Lys-Asn-Thr-Leu-Tyr-Leu-Gln-Met-Asn-Ser-Leu-Arg-Ala-Glu-Asp-Thr-Ala-Val-Tyr-Tyr-Cys-Ala-Lys-/CDR/-Trp-Gly-Gln-Gly-Thr-Leu-Val-Thr-Val-Ser-Ser, CDR indicating the presence of a CDR of which at least one is (a), (b) or (c) or a conservatively modified variant thereof.

10. An aglycosylated antibody according to Claim 8 or 9, in which the light chain variable domain framework region reading in the leader → constant domain direction comprises

Asp-Phe-Met-Leu-Thr-Gln-Pro-His-Ser-Val-Ser-Glu-Ser-Pro-Gly-Lys-Thr-Val-Ile-Ile-Ser-Cys-/CDR/-Trp-Tyr-Gln-Gln-Arg-Pro-Gly-Arg-Ala-Pro-Thr-Thr-Val-Ile-Phe-/CDR/-Gly-Val-Pro-Asp-Arg-Phe-Ser-Gly-Ser-Ile-Asp-Arg-Ser-Ser-Asn-Ser-Ala-Ser-Leu-Thr-Ile-Ser-Gly-Leu-Gln-Thr-Glu-Asp-Glu-Ala-Asp-Tyr-Tyr-Cys-/CDR/-Phe-Gly-Gly-Gly-Thr-Lys-Leu-Thr-Val-Leu-Gly-Gln-Pro-Lys-Ala-Ala-Pro-Ser-Val-Thr-Leu-Phe-Pro-Pro-Ser-Ser-Glu-Glu-Leu-Gln, CDR indicating the presence of a CDR of which at least one is (d), (e) or (f) or a conservatively modified variant thereof.

11. An aglycosylated antibody according to Claim 9 having a heavy chain variable domain which comprises

Glu-Val-Gln-Leu-Leu-Glu-Ser-Gly-Gly-Gly-Leu-Val-Gln-Pro-Gly-Gly-Ser-Leu-Arg-Leu-Ser-Cys-Ala-Ala-Ser-Gly-Phe-Thr-Phe-Ser-Ser-Phe-Pro-Met-Ala-Trp-Val-Arg-Gln-Ala-Pro-Gly-Lys-Gly-Leu-Glu-Trp-Val-Ser-Thr-Ile-Ser-Thr-Ser-Gly-Gly-Arg-Thr-Tyr-Tyr-Arg-Asp-Ser-Val-Lys-Gly-Arg-Phe-Thr-Ile-Ser-Arg-Asp-Asn-Ser-Lys-Asn-Thr-Leu-Tyr-Leu-Gln-Met-Asn-Ser-Leu-Arg-Ala-Glu-Asp-Thr-Ala-Val-Tyr-Tyr-Cys-Ala-Lys-Phe-Arg-Gln-Tyr-Ser-Gly-Gly-Phe-Asp-Tyr-Trp-Gly-Gln-Gly-Thr-Leu-Val-Thr-Val-Ser-Ser.

12. An aglycosylated antibody according to Claim 8 or 11 having a light chain variable domain which comprises

Asp-Phe-Met-Leu-Thr-Gln-Pro-His-Ser-Val-Ser-Glu-Ser-Pro-Gly-Lys-Thr-Val-Ile-Ile-Ser-Cys-Thr-Leu-Ser-Ser-Gly-Asn-Ile-Glu-Asn-Asn-Tyr-Val-His-Trp-Tyr-Gln-Gln-Arg-Pro-Gly-Arg-Ala-Pro-Thr-Thr-Val-Ile-Phe-Asp-Asp-Asp-Lys-Arg-Pro-Asp-Gly-Val-Pro-Asp-Arg-Phe-Ser-Gly-Ser-Ile-Asp-Arg-Ser-Ser-Asn-Ser-Ala-Ser-Leu-Thr-Ile-Ser-Gly-Leu-Gln-Thr-Glu-Asp-Glu-Ala-Asp-Tyr-Tyr-Cys-His-Ser-Tyr-Val-Ser-Ser-Phe-Asn-Val-Phe-Gly-Gly-Gly-Thr-Lys-Leu-Thr-Val-Leu-Gly-Gln-Pro-Lys-Ala-Ala-Pro-Ser-Val-Thr-Leu-Phe-Pro-Pro-Ser-Ser-Glu-Glu-Leu-Gln.

13. An aglycosylated antibody according to any of Claims 1 to 12, in which the constant domains are of or are derived from those of rat or mouse origin.
14. An aglycosylated antibody according to any of Claims 1 to 12, in which the CDRs are of different origin to the constant region.
15. An aglycosylated antibody according to any of Claims 1 to 12, in which the constant domains are of or are derived from those of human origin.
16. An aglycosylated antibody according to any of Claims 1 to 15, in which the constant region is of an IgG isotype.
17. An aglycosylated antibody according to Claim 15, in which the constant region is of an IgG1 isotype.
18. An aglycosylated antibody according to Claim 15, 16 or 17, in which asparagine residue at position 297 of each constant region heavy chain is replaced by an alternative amino acid residue.
19. An aglycosylated antibody according to Claim 18, in which the asparagine residue is replaced by an alanine residue.
20. An aglycosylated antibody according to any of the preceding claims, in which only one of the arms thereof has an affinity for the CD3 antigen.
21. An aglycosylated antibody according to Claim 20 which is monovalent.
22. An aglycosylated antibody according to Claim 21, in which one half of the antibody consists of a complete heavy chain and light chain and the other half consists of a similar but truncated heavy chain lacking the binding site for the light chain.
23. An aglycosylated antibody according to any of Claims 1 to 22 in the form of a pharmaceutical composition comprising a physiologically acceptable diluent or carrier.
24. An aglycosylated antibody according to any of Claims 1 to 22, for use in therapy.
25. The use of an aglycosylated antibody according to any of Claims 1 to 22 for the manufacture of a medicament for use in immunosuppression.

26. The use according to Claim 25, in which the medicament is for use in the treatment of recipients of a transplant.

05 27. A method of treating a patient having cancer or requiring immunosuppression which comprises administering to said patient a therapeutically effective amount of a ligand or an antibody or fragment thereof according to any of Claims 1 to 22.

135511/PCT/14